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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/358,755	07/22/1999	HIROSHI KAWABATA	008708-D7024	1939

7590 04/09/2004

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 04/09/2004

Re Mail

Please find below and/or attached an Office communication concerning this application or proceeding.



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26021 7590 02/25/2003				
HOGAN & HARTSON L.L.P. 500 S. GRAND AVENUE SUITE 1900 LOS ANGELES, CA 90071-2611				
EXAMINER MURPHY, JOSEPH F				
ART UNIT		PAPER NUMBER		
1646		# 29		

DATE MAILED: 02/25/2003

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**Office Action Summary**

Application No.

09/358,755

Applicant(s)

KAWABATA ET AL.

Examiner

Joseph F Murphy

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 12-18, 20-23, 43-58 and 60-70 is/are pending in the application.
- 4a) Of the above claim(s) 12-18 and 20-23 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 32, 43-58 and 60 is/are allowed.
- 6) ☒ Claim(s) 63-70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

Art Unit: 1646

## DETAILED ACTION

### *Formal Matters*

Claims 12-18, 20-23, 43-58, 60-70 are pending. Claims 12-18, 20-23 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 43-58, 60-70 are under consideration.

### *Response to Arguments*

Applicant's arguments filed 11/12/2002 have been fully considered but they are not persuasive, for the reasons set forth below.

### *Claim Rejections - 35 USC § 112 first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 63-70 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleotide sequence consisting of SEQ ID NO: 2 and SEQ ID NO: 3, does not reasonably provide enablement for a nucleotide sequence consisting of a sequence which is 60% identical to SEQ ID NO: 2 and SEQ ID NO: 3, for reasons of record set forth in Paper No. 26, 10/22/2002. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 63 is overly broad in the recitation of "60% identical " since insufficient guidance is provided as to which of the myriad of polynucleotide species encompassed by the claim will encode proteins which retain the characteristics of TfR. In the specification (page 8, lines 15), Applicants disclose that variants of the polynucleotide have sufficient homology to the reference

Art Unit: 1646

polynucleotide such that it will hybridize under moderate conditions, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible encoded muteins of TfR. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is insufficient guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding TfR other than those exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

Art Unit: 1646

(1) the breadth of the claims - The claims included in the instant rejection are drawn to a nucleotide sequence consisting of a sequence which is 60% identical to SEQ ID NO: 2 and SEQ ID NO: 3.

(2) the nature of the invention - The instant invention is a nucleic acid encoding a protein.

(3) the state of the prior art - The Mikayama and Voet references demonstrate that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the encoded protein's function.

(5) the level of predictability in the art - The Mikayama and Voet references demonstrate the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has only taught SEQ ID NO: 2 and SEQ ID NO: 3, which are 82.6% identical, and not a nucleotide sequence consisting of a sequence which is 60% identical to SEQ ID NO: 2 and SEQ ID NO: 3 that encode TfR polypeptides.

(7) the existence of working examples - Working examples are provided only for the protein encoded by SEQ ID NO: 2 and 3, which are 82.6% identical.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Since the claims encompass a nucleotide sequence consisting of a sequence which is 60% identical to SEQ ID NO: 2 and SEQ ID NO: 3, and guidance is provided only for nucleic acids which are 82.6% identical, it would require the skilled artisan to determine which are the encoded amino acid residues which are necessary for TfR function to make and use the claimed invention.

Art Unit: 1646

Given the breadth of claims 63-70 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Applicant argues that the standard for enablement has been met as long as Applicant discloses at least one method for making and using the claimed invention, that the specification discloses methods which may be used to describe the claimed sequences, and that experimentation is permissible while still satisfying the enablement requirement. However, As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case there are a large number of nucleic acid sequences which are 60% identical to SEQ ID NO: 2, however, these encode unrelated proteins.



Art Unit: 1646

Therefore, the does not provide the necessary guidance for one of skill in the art to use the nucleic acid sequences which do not encode a transferrin binding protein. Additionally, the specification does not disclose the critical residues necessary to maintain function. The specification does not disclose the correlation between the structure (sequence) of the polypeptides and the function of binding transferrin. The amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the nucleic acids encoding polypeptides are lacking, it is unpredictable as to which encoding variations, if any, meet the limitations of the claims. Therefore it would require undue experimentation by one of skill in the art to make and use the invention as claimed without further guidance from the instant specification.

### ***Conclusion***

Claims 63-70 are rejected.

Claims 43-58, 60-62 are allowable.

Art Unit: 1646


*Advisory Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245.


The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
February 20, 2003



YVONNE EYLER, PH.D.  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600